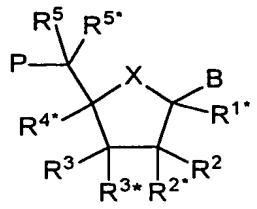
CLAIMS

1. An oligomer (hereinafter termed "LNA modified oligonucleotide") comprising at least one nucleoside analogue (hereinafter termed "LNA") of the general formula I



I

wherein X is selected from -O-, -S-, -N(R^{N*})-, -C(R^6R^{6*})-, -O-C(R^7R^{7*})-, -C(R^6R^{6*})-O-, -S-C(R^7R^{7*})-, -C(R^6R^{6*})-S-, -N(R^{N*})-C(R^7R^{7*})-, -C(R^6R^{6*})-N(R^{N*})-, and -C(R^6R^{6*})-C(R^7R^{7*})-;

B is selected from hydrogen, hydroxy, optionally substituted C_{1-4}-alkoxy, optionally substituted C_{1-4}-alkyl, optionally substituted C_{1-4}-acyloxy, nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

P designates the radical position for an internucleoside linkage to a succeeding monomer, or a 5'-terminal group, such internucleoside linkage or 5'-terminal group optionally including the substituent R^5;

one of the substituents R^2, R^{2*}, R^3, and R^{3*} is a group P* which designates an internucleoside linkage to a preceding monomer, or a 3'-terminal group;

one or two pairs of non-geminal substituents selected from the present substituents of R^{1*}, R^{4*}, R^5, R^{5*}, R^6, R^{6*}, R^7, R^{7*}, R^{N*}, and the ones of R^2, R^{2*}, R^3, and R^{3*} not designating P* each designates a biradical consisting of 1-8 groups/atoms selected from -C(R^aR^b)-, -C(R^a)=C(R^a)-, -C(R^a)=N-, -O-, -Si(R^a)$_2$-, -S-, -SO_2-, -N(R^a)-, and >C=Z,

wherein Z is selected from -O-, -S-, and -N(R^a)-, and R^a and R^b each is independently selected from hydrogen, optionally substituted C_{1-12}-alkyl, optionally substituted C_{2-12}-alkenyl, optionally substituted C_{2-12}-alkynyl, hydroxy, C_{1-12}-alkoxy, C_{2-12}-alkenyloxy, carboxy, C_{1-12}-alkoxycarbonyl, C_{1-12}-alkylcarbonyl,

formyl, aryl, aryloxy-carbonyl, aryloxy, arylcarbonyl, heteroaryl, heteroaryloxy-carbonyl, heteroaryloxy, heteroarylcarbonyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, amino-C_{1-6}-alkyl-aminocarbonyl, mono- and di(C_{1-6}-alkyl)amino-C_{1-6}-alkyl-aminocarbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, C_{1-6}-alkanoyloxy, sulphono, C_{1-6}-alkylsulphonyloxy, nitro, azido, sulphanyl, C_{1-6}-alkylthio, halogen, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, where aryl and heteroaryl may be optionally substituted, and where two geminal substituents R^a and R^b together may designate optionally substituted methylene ($=CH_2$), and wherein two non-geminal or geminal substitutents selected from R^a, R^b, and any of the substituents R^{1*}, R^2, R^{2*}, R^3, R^{3*}, R^{4*}, R^5, R^{5*}, R^6 and R^{6*}, R^7, and R^{7*} which are present and not involved in P, P^* or the biradical(s) together may form an associated biradical selected from biradicals of the same kind as defined before; said pair(s) of non-geminal substituents thereby forming a mono- or bicyclic entity together with (i) the atoms to which said non-geminal substituents are bound and (ii) any intervening atoms; and

each of the substituents R^{1*}, R^2, R^{2*}, R^3, R^{4*}, R^5, R^{5*}, R^6 and R^{6*}, R^7, and R^{7*} which are present and not involved in P, P^* or the biradical(s), is independently selected from hydrogen, optionally substituted C_{1-12}-alkyl, optionally substituted C_{2-12}-alkenyl, optionally substituted C_{2-12}-alkynyl, hydroxy, C_{1-12}-alkoxy, C_{2-12}-alkenyloxy, carboxy, C_{1-12}-alkoxycarbonyl, C_{1-12}-alkylcarbonyl, formyl, aryl, aryloxy-carbonyl, aryloxy, arylcarbonyl, heteroaryl, heteroaryloxy-carbonyl, heteroaryloxy, heteroarylcarbonyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, amino-C_{1-6}-alkyl-aminocarbonyl, mono- and di(C_{1-6}-alkyl)amino-C_{1-6}-alkyl-aminocarbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, C_{1-6}-alkanoyloxy, sulphono, C_{1-6}-alkylsulphonyloxy, nitro, azido, sulphanyl, C_{1-6}-alkylthio, halogen, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, where aryl and heteroaryl may be optionally substituted, and where two geminal substituents together may designate oxo, thioxo, imino, or optionally substituted methylene, or together may form a spiro biradical consisting of a 1-5 carbon atom(s) alkylene chain which is optionally interrupted and/or terminated by one or more heteroatoms/groups selected from -O-, -S-, and -(NR^N)- where R^N is

selected from hydrogen and C_{1-4}-alkyl, and where two adjacent (non-geminal) substituents may designate an additional bond resulting in a double bond; and R^{N*}, when present and not involved in a biradical, is selected from hydrogen and C_{1-4}-alkyl;

and basic salts and acid addition salts thereof;

with the proviso that,

(i) R^3 and R^5 do not together designate a biradical selected from $-CH_2-CH_2-$, $-O-CH_2-$, when LNA is a bicyclic nucleoside analogue;

(ii) R^3, R^5, and R^{5*} do not together designate a triradical $-CH_2-CH(-)-CH_2-$ when LNA is a tricyclic nucleoside analogue;

(iii) R^{1*} and R^{6*} do not together designate a biradical $-CH_2-$ when LNA is a bicyclic nucleoside analogue; and

(iv) R^{4*} and R^{6*} do not together designate a biradical $-CH_2-$ when LNA is a bicyclic nucleoside analogue.

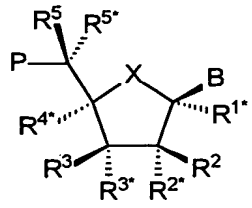
2. An oligomer according to claim 1, wherein the one or two pairs of non-geminal substituents, constituting one or two biradical(s), respectively, are selected from the present substituents of R^{1*}, R^{4*}, R^6, R^{6*}, R^7, R^{7*}, R^{N*}, and the ones of R^2, R^{2*}, R^3, and R^{3*} not designating P^*.

3. An oligomer according to claim 1, comprising 1-10000 LNA(s) of the general formula I and 0-10000 nucleosides selected from naturally occurring nucleosides and nucleoside analogues, with the proviso that the sum of the number of nucleosides and the number of LNA(s) is at least 2.

4. An oligomer according to claim 3, wherein at least one LNA comprises a nucleobase as the substituent B.

5. An oligomer according to claim 1, wherein one of the substituents R^3 and R^{3*} designates P^*.

6. An oligomer according to claim 1, wherein the LNA(s) has/have the following formula Ia



Ia

wherein P, P*, B, X, R^{1*}, R^2, R^{2*}, R^3, R^{4*}, R^5, and R^{5*} are as defined in claim 1.

7. An oligomer according to claim 6, wherein R^{3*} designates P*.

8. An oligomer according to claim 1, comprising one biradical constituted by a pair of (two) non-geminal substituents.

9. An oligomer according to claim 1, wherein X is selected from $-(CR^6R^{6*})-$, -O-, -S-, and $-N(R^{N*})-$.

10. An oligomer according to claim 1, wherein the biradical(s) constituted by pair(s) of non-geminal substituents is/are selected from $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-Y-$, $-Y-(CR^*R^*)_{r+s}-Y-$, $-Y-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, $-(CR^*R^*)_{r+s}-$, -Y-, -Y-Y-, wherein each Y is independently selected from -O-, -S-, $-Si(R^*)_2-$, $-N(R^*)-$, $>C=O$, $-C(=O)-N(R^*)-$, and $-N(R^*)-C(=O)-$, each R^* is independently selected from hydrogen, halogen, azido, cyano, nitro, hydroxy, mercapto, amino, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and/or two adjacent (non-geminal) R^* may together designate a double bond, and each of r and s is 0-4 with the proviso that the sum r+s is 1-5.

11. An oligomer according to claim 10, wherein each biradical is independently selected from -Y-, $-(CR^*R^*)_{r+s}-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, and $-Y-(CR^*R^*)_{r+s}-Y-$, wherein and each of r and s is 0-3 with the proviso that the sum r+s is 1-4.

12. An oligomer according to claim 11, wherein

(i) R^{2*} and R^{4*} together designate a biradical selected from -Y-, $-(CR^*R^*)_{r+s+1}-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, and $-Y-(CR^*R^*)_{r+s}-Y-$;

(ii) R^2 and R^3 together designate a biradical selected from -Y-, $-(CR^*R^*)_{r+s}-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, and $-Y-(CR^*R^*)_{r+s}-Y-$;

(iii) R^{2*} and R^3 together designate a biradical selected from -Y-, $-(CR^*R^*)_{r+s}-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, and $-Y-(CR^*R^*)_{r+s}-Y-$;

(iv) R^3 and R^{4*} together designate a biradical selected from -Y-, $-(CR^*R^*)_{r+s}-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, and $-Y-(CR^*R^*)_{r+s}-Y-$;

(v) R^3 and R^5 together designate a biradical selected from -Y'-, $-(CR^*R^*)_{r+s+1}-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, and $-Y-(CR^*R^*)_{r+s}-Y-$;

(vi) R^{1*} and R^{4*} together designate a biradical selected from -Y'-, $-(CR^*R^*)_{r+s+1}-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, and $-Y-(CR^*R^*)_{r+s}-NR^*-$; or

(vii) R^{1*} and R^{2*} together designate a biradical selected from -Y-, $-(CR^*R^*)_{r+s}-$, $-(CR^*R^*)_r-Y-(CR^*R^*)_s-$, and $-Y-(CR^*R^*)_{r+s}-Y-$;

wherein each of r and s is 0-3 with the proviso that the sum r+s is 1-4, and where Y' is selected from $-NR^*-C(=O)-$ and $-C(=O)-NR^*-$.

13. An oligomer according to claim 12, wherein one of the following criteria applies for at least one LNA:

(i) R^{2*} and R^{4*} together designate a biradical selected from -O-, -S-, $-N(R^*)-$, $-(CR^*R^*)_{r+s+1}-$, $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$, $-O-(CR^*R^*)_{r+s}-O-$, $-S-(CR^*R^*)_{r+s}-O-$, $-O-(CR^*R^*)_{r+s}-S-$, $-N(R^*)-(CR^*R^*)_{r+s}-O-$, $-O-(CR^*R^*)_{r+s}-N(R^*)-$, $-S-(CR^*R^*)_{r+s}-S-$, $-N(R^*)-(CR^*R^*)_{r+s}-N(R^*)-$, $-N(R^*)-(CR^*R^*)_{r+s}-S-$, and $-S-(CR^*R^*)_{r+s}-N(R^*)-$;

(ii) R^2 and R^3 together designate a biradical selected from -O-, $-(CR^*R^*)_{r+s}-$, $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

(iii) R^{2*} and R^3 together designate a biradical selected from -O-, $-(CR^*R^*)_{r+s}-$, $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

(iv) R^3 and R^{4*} together designate a biradical selected from $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

(v) R^3 and R^5 together designate a biradical selected from $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$; or

(vi) R^{1*} and R^{4*} together designate a biradical selected from $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

(vii) R^{1*} and R^{2*} together designate a biradical selected from $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

wherein each of r and s is 0-3 with the proviso that the sum r + s is 1-4, and where X is selected from -O-, -S-, and $-N(R^H)-$ where R^H designates hydrogen or C_{1-4}-alkyl.

14. An oligomer according to claim 13, wherein R^{3*} designates P^*.

15. An oligomer according to claim 14, wherein R^{2*} and R^{4*} together designate a biradical.

16. An oligomer according to claim 15, wherein X is O, R^2 is selected from hydrogen, hydroxy, and optionally substituted C_{1-6}-alkoxy, and R^{1*}, R^3, R^5, and R^{5*} designate hydrogen.

17. An oligomer according to claim 16, wherein the biradical is selected from –O-, $-(CH_2)_{0-1}-O-(CH_2)_{1-3}-$, $-(CH_2)_{0-1}-S-(CH_2)_{1-3}-$, and $-(CH_2)_{0-1}-N(R^N)-(CH_2)_{1-3}-$.

18. An oligomer according to claim 17, wherein the biradical is selected from $-O-CH_2-$, $-S-CH_2-$ and $-N(R^N)-CH_2-$.

19 An oligomer according to claim 15, wherein B is selected from nucleobases.

20. An oligomer according to claim 19, wherein the oligomer comprises at least one LNA wherein B is selected from adenine and guanine and at least one LNA wherein B is selected from thymine, cytosine and uracil.

21. An oligomer according to claim 16, wherein the biradical is $-(CH_2)_{2-4}-$.

22. An oligomer according to claim 14, wherein R^2 and R^3 together designate a biradical.

23. An oligomer according to claim 22, wherein X is O, R^{2*} is selected from hydrogen, hydroxy, and optionally substituted C_{1-6}-alkoxy, and R^{1*}, R^{4*}, R^5, and R^{5*} designate hydrogen.

24. An oligomer according to claim 23, wherein the biradical is $-(CH_2)_{0-1}-O-(CH_2)_{1-3}-$.

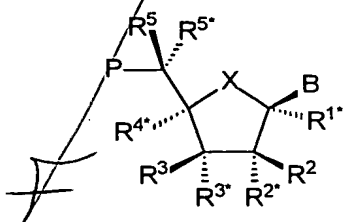
25. An oligomer according to claim 23, wherein the biradical is $-(CH_2)_{1-4}-$.

26. An oligomer according to claim 14, wherein one R^* is selected from hydroxy, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and any remaining substituents R^* are hydrogen.

27. An oligomer according to claim 14, wherein a group R^* in the biradical of at least one LNA is selected from DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands.

28. An oligomer according to claim 14, wherein the LNA(s) has/have the general formula Ia.

29. An oligomer according to claim 1 of the general formula Ia



Ia

wherein X is -O-;

B is selected from nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

P designates the radical position for an internucleoside linkage to a succeeding monomer, or a 5'-terminal group, such internucleoside linkage or 5'-terminal group optionally including the substituent R^5;

R^{3*} is a group P* which designates an internucleoside linkage to a preceding monomer, or a 3'-terminal group;

R^{2*} and R^{4*} together designate a biradical selected from -O-, -S-, -N(R^*)-, -($CR^*R^*)_{r+s+1}$-, -($CR^*R^*)_r$-O-($CR^*R^*)_s$-, -($CR^*R^*)_r$-S-($CR^*R^*)_s$-, -($CR^*R^*)_r$-N(R^*)-($CR^*R^*)_s$-, -O-($CR^*R^*)_{r+s}$-O-, -S-($CR^*R^*)_{r+s}$-O-, -O-($CR^*R^*)_{r+s}$-S-, -N(R^*)-($CR^*R^*)_{r+s}$-O-, -O-($CR^*R^*)_{r+s}$-N(R^*)-, -S-($CR^*R^*)_{r+s}$-S-, -N(R^*)-($CR^*R^*)_{r+s}$-N(R^*)-, -N(R^*)-($CR^*R^*)_{r+s}$-S-, and -S-($CR^*R^*)_{r+s}$-N(R^*)-; wherein each R^* is independently selected from hydrogen, halogen, azido, cyano, nitro, hydroxy, mercapto, amino, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and/or two adjacent (non-geminal) R^* may together designate a double bond, and each of r and s is 0-3 with the proviso that the sum r+s is 1-4;each of the substituents R^{1*}, R^2, R^3, R^5, and R^{5*} is independently selected from hydrogen, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, hydroxy, C_{1-6}-alkoxy, C_{2-6}-alkenyloxy, carboxy, C_{1-6}-alkoxycarbonyl, C_{1-6}-alkylcarbonyl, formyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, azido, C_{1-6}-alkanoyloxy, sulphono, sulphanyl, C_{1-6}-alkylthio, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and halogen, where two geminal substituents together may designate oxo;

and basic salts and acid addition salts thereof.

30. An oligomer according to claim 29, wherein one R^* is selected from hydrogen, hydroxy, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and any remaining substituents R^* are hydrogen.

31. An oligomer according to claim 29, wherein the biradical is selected from -O-, $-(CH_2)_{0-1}-O-(CH_2)_{1-3}-$, $-(CH_2)_{0-1}-S-(CH_2)_{1-3}-$, $-(CH_2)_{0-1}-N(R^N)-(CH_2)_{1-3}-$, and $-(CH_2)_{2-4}-$.

32. An oligomer according to claim 31, wherein the biradical is selected from $-O-CH_2-$, $-S-CH_2-$ and $-N(R^N)-CH_2-$.

33. An oligomer according to claim 29, wherein B is selected from nucleobases.

34. An oligomer according to claim 33, wherein the oligomer comprises at least one LNA wherein B is selected from adenine and guanine and at least one LNA wherein B is selected from thymine, cytosine and urasil.

35. An oligomer according to claim 29, wherein R^2 is selected from hydrogen, hydroxy and optionally substituted C_{1-6}-alkoxy, and R^{1*}, R^3, R^5, and R^{5*} designate hydrogen.

36. An oligomer according to claim 1, wherein any internucleoside linkage of the LNA(s) is selected from linkages consisting of 2 to 4 groups/atoms selected from $-CH_2-$, -O-, -S-, $-NR^H-$, $>C=O$, $>C=NR^H$, $>C=S$, $-Si(R'')_2-$ -SO-, $-S(O)_2-$, $-P(O)_2-$, -P(O,S)-, $-P(S)_2-$, -PO(R'')-, $-PO(OCH_3)-$, and $-PO(NHR^H)-$, where R^H is selected form hydrogen and C_{1-4}-alkyl, and R'' is selected from C_{1-6}-alkyl and phenyl.

37. An oligomer according to claim 36, wherein any internucleoside linkage of the LNA(s) is selected from $-CH_2-CH_2-CH_2-$, $-CH_2-CO-CH_2-$, $-CH_2-CHOH-CH_2-$, $-O-CH_2-O-$, $-O-CH_2-CH_2-$, $-O-CH_2-CH=$, $-CH_2-CH_2-O-$, $-NR^H-CH_2-CH_2-$, $-CH_2-CH_2-NR^H-$, $-CH_2-NR^H-CH_2-$, $-O-CH_2-CH_2-NR^H-$, $-NR^H-CO-O-$, $-NR^H-CO-NR^H-$, $-NR^H-CS-NR^H-$, $-NR^H-C(=NR^H)-NR^H-$, $-NR^H-CO-CH_2-NR^H-$, $-O-CO-O-$, $-O-CO-CH_2-O-$, $-O-CH_2-CO-O-$, $-CH_2-CO-NR^H-$, $-O-CO-NR^H-$, $-NR^H-CO-CH_2-$, $-O-CH_2-CO-NR^H-$, $-O-CH_2-CH_2-NR^H-$, $-CH=N-O-$, $-CH_2-NR^H-O-$, $-CH_2-O-N=$, $-CH_2-O-NR^H-$, $-CO-NR^H-CH_2-$, $-CH_2-NR^H-O-$, $-CH_2-NR^H-CO-$, $-O-NR^H-CH_2-$, $-O-NR^H-$, $-O-CH_2-S-$, $-S-CH_2-O-$, $-CH_2-CH_2-S-$, $-O-CH_2-CH_2-S-$, $-S-CH_2-CH=$, $-S-CH_2-CH_2-$, $-S-CH_2-CH_2-O-$, $-S-CH_2-CH_2-S-$, $-CH_2-S-CH_2-$, $-CH_2-SO-CH_2-$, $-CH_2-SO_2-CH_2-$, -O-SO-O-, $-O-S(O)_2-O-$, $-O-S(O)_2-CH_2-$, $-O-S(O)_2-NR^H-$, $-NR^H-S(O)_2-CH_2-$, $-O-S(O)_2-CH_2-$, $-O-P(O)_2-O-$, -O-P(O,S)-O-, $-O-P(S)_2-O-$, $-S-P(O)_2-O-$, -S-P(O,S)-O-, $-S-P(S)_2-O-$, $-O-P(O)_2-S-$, -O-P(O,S)-S-, $-O-P(S)_2-S-$, $-S-P(O)_2-S-$, -S-P(O,S)-S-, $-S-P(S)_2-S-$,

-O-PO(R'')-O-, -O-PO(OCH_3)-O-, -O-PO(BH_3)-O-, -O-PO(NHR^N)-O-, -O-P(O)$_2$-NR^H-, -NR^H-P(O)$_2$-O-, -O-P(O,NR^H)-O-, and -O-Si(R'')$_2$-O-.

38. An oligomer according to claim 37, wherein any internucleoside linkage of the LNA(s) is selected from -CH_2-CO-NR^H-, -CH_2-NR^H-O-, -S-CH_2-O-, -O-P(O)$_2$-O-, -O-P(O,S)-O-, -O-P(S)$_2$-O-, -NR^H-P(O)$_2$-O-, -O-P(O,NR^H)-O-, -O-PO(R'')-O-, -O-PO(CH_3)-O-, and -O-PO(NHR^N)-O-, where R^H is selected form hydrogen and C_{1-4}-alkyl, and R'' is selected from C_{1-6}-alkyl and phenyl.

39. An oligomer according to claim 1, wherein each of the substituents R^{1*}, R^2, R^{2*}, R^3, R^{3*}, R^{4*}, R^5, R^{5*}, R^6, R^{6*}, R^7, and R^{7*} of the LNA(s), which are present and not involved in P, P* or the biradical(s), is independently selected from hydrogen, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, hydroxy, C_{1-6}-alkoxy, C_{2-6}-alkenyloxy, carboxy, C_{1-6}-alkoxycarbonyl, C_{1-6}-alkylcarbonyl, formyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, azido, C_{1-6}-alkanoyloxy, sulphono, sulphanyl, C_{1-6}-alkylthio, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and halogen, where two geminal substituents together may designate oxo, and where R^{N*}, when present and not involved in a biradical, is selected from hydrogen and C_{1-4}-alkyl.

40. An oligomer according to claim 1, wherein X is selected from -O-, -S-, and -NR^{N*}-, and each of the substituents R^{1*}, R^2, R^{2*}, R^3, R^{3*}, R^{4*}, R^5, R^{5*}, R^6, R^{6*}, R^7, and R^{7*} of the LNA(s), which are present and not involved in P, P* or the biradical(s), designate hydrogen.

41. An oligomer according to claim 1, wherein P is a 5'-terminal group selected from hydrogen, hydroxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkylcarbonyloxy, optionally substituted aryloxy, monophosphate, diphosphate, triphosphate, and -W-A', wherein W is selected from -O-, -S-, and -N(R^H)- where R^H is selected from hydrogen and C_{1-6}-alkyl, and where A' is selected from DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands.

42. An oligomer according to claim 1, wherein P* is a 3'-terminal group selected from hydrogen, hydroxy, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkylcarbonyloxy, optionally substituted aryloxy, and -W-A', wherein W is selected from -O-, -S-, and -N(R^H)- where R^H is selected from hydrogen and C_{1-6}-alkyl, and where A' is selected from DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands.

43. An oligomer according to claims 1, having the following formula V:

$$G\text{-}[Nu\text{-}L]_{n(0)}\text{-}\{[LNA\text{-}L]_{m(q)}\text{-}[Nu\text{-}L]_{n(q)}\}_q\text{-}G^* \qquad V$$

wherein

q is 1-50;

each of n(0), .., n(q) is independently 0-10000;

each of m(1), .., m(q) is independently 1-10000;

with the proviso that the sum of n(0), .., n(q) and m(1), .., m(q) is 2-15000;

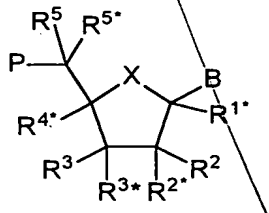
G designates a 5'-terminal group;

each Nu independently designates a nucleoside selected from naturally occurring nucleosides and nucleoside analogues;

each LNA independently designates a nucleoside analogue;

each L independently designates an internucleoside linkage between two groups selected from Nu and LNA, or L together with G* designates a 3'-terminal group; and

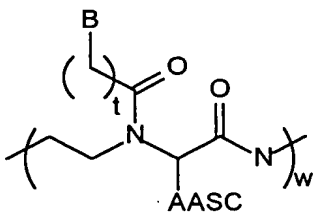
each LNA-L independently designates a nucleoside analogue of the general formula I:



I

wherein the substituents B, P, P*, R^{1*}, R^2, R^{2*}, R^3, R^{4*}, R^5, and R^{5*}, and X are as defined in claim 1.

44. An oligomer according to claim 1, further comprising a PNA mono- or oligomer segment of the formula



wherein B is a defined above for the formula I, AASC designates hydrogen or an amino acid side chain, t is 1-5, and w is 1-50.

45. An oligomer according to claim 1, which has an increased specificity towards complementary ssRNA or ssDNA compared to the native oligonucleotide.

46. An oligomer according to claim 1, which has an increased affinity towards complementary ssRNA or ssDNA compared to the native oligonucleotide.

47. An oligomer according to claim 1, which is capable of binding to a target sequence in a dsDNA or dsRNA molecule by way of "strand displacement" or by triple helix formation.

48. An oligomer according to claim 1, which is more resistant to nucleases than the native oligonucleotide.

49. An oligomer according to claim 1, which has nucleic acid catalytic activity (LNA modified ribozymes).

50. An oligomer comprising at least one nucleoside analogue which imparts to the oligomer a T_m with a complementary DNA oligonucleotide which is at least 2.5 °C higher than that of the corresponding unmodified reference oligonucleotide which does not comprise any nucleoside analogue.

51. An oligomer according to claim 50, wherein the T_m is at least 2.5 x N °C higher, where N is the number of nucleoside analogues.

52. An oligomer comprising at least one nucleoside analogue which imparts to the oligomer a T_m with a complementary RNA oligonucleotide which is at least 4.0 °C

higher than that of the corresponding unmodified reference oligonucleotide which does not comprise any nucleoside analogue.

53. An oligomer according to claim 52, wherein the T_m is at least 4.0 x N °C higher, where N is the number of nucleoside analogues.

54. An oligomer according to claim 50 or 52, wherein the oligomer is as defined in claim 1, where the at least one nucleoside analogue has the formula I where B is a nucleobase.

55. An oligomer according to claim 50, wherein said oligomer, when hybridised with a partially complementary DNA oligonucleotide having one or more mismatches with said oligomer, exhibits a reduction in T_m, as a result of said mismatches, which is equal to or greater than the reduction which would be observed with the corresponding unmodified reference oligonucleotide which does not comprise any nucleoside analogues.

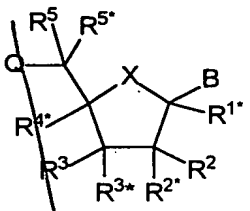
56. An oligomer according to claim 52, wherein said oligomer, when hybridised with a partially complementary RNA oligonucleotide having one or more mismatches with said oligomer, exhibits a reduction in T_m, as a result of said mismatches, which is equal to or greater than the reduction which would be observed with the corresponding unmodified reference oligonucleotide which does not comprise any nucleoside analogues.

57. An oligomer according to claim 50 or 52, which has substantially the same sensitivity of T_m to the ionic strength of the hybridisation buffer as that of the corresponding unmodified reference oligonucleotide.

58. An oligomer according to claim 50 or 52, which is at least 30% modified.

59. An oligomer according to claim 50 or 52, which has substantially higher 3'-exonucleolytic stability than the corresponding unmodified reference oligonucleotide.

60. A nucleoside analogue (hereinafter LNA) of the general formula II



II

wherein the substituent B is selected from nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

X is selected from -O-, -S-, -N(R^{N*})-, and -C(R^6R^{6*})-;

one of the substituents R^2, R^{2*}, R^3, and R^{3*} is a group Q*;

each of Q and Q* is independently selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Prot-O-, Act-O-, mercapto, Prot-S-, Act-S-, C_{1-6}-alkylthio, amino, Prot-N(R^H)-, Act-N(R^H)-, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyl, optionally substituted C_{2-6}-alkynyloxy, monophosphate, diphosphate, triphosphate, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, carboxy, sulphono, hydroxymethyl, Prot-O-CH_2-, Act-O-CH_2-, aminomethyl, Prot-N(R^H)-CH_2-, Act-N(R^H)-CH_2-, carboxymethyl, sulphonomethyl, where Prot is a protection group for -OH, -SH, and -NH(R^H), respectively, Act is an activation group for -OH, -SH, and -NH(R^H), respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl;

(i) R^{2*} and R^{4*} together designate a biradical selected from -O-, -(CR^*R^*)$_{r+s+1}$-, -(CR^*R^*)$_r$-O-(CR^*R^*)$_s$-, -(CR^*R^*)$_r$-S-(CR^*R^*)$_s$-, -(CR^*R^*)$_r$-N(R^*)-(CR^*R^*)$_s$-, -O-(CR^*R^*)$_{r+s}$-O-, -S-(CR^*R^*)$_{r+s}$-O-, -O-(CR^*R^*)$_{r+s}$-S-, -N(R^*)-(CR^*R^*)$_{r+s}$-O-, -O-(CR^*R^*)$_{r+s}$-N(R^*)-, -S-(CR^*R^*)$_{r+s}$-S-, -N(R^*)-(CR^*R^*)$_{r+s}$-N(R^*)-, -N(R^*)-(CR^*R^*)$_{r+s}$-S-, and -S-(CR^*R^*)$_{r+s}$-N(R^*)-;

(ii) R^2 and R^3 together designate a biradical selected from -O-, -(CR^*R^*)$_{r+s}$-, -(CR^*R^*)$_r$-O-(CR^*R^*)$_s$-, -(CR^*R^*)$_r$-S-(CR^*R^*)$_s$-, and -(CR^*R^*)$_r$-N(R^*)-(CR^*R^*)$_s$-;

(iii) R^{2*} and R^3 together designate a biradical selected from -O-, $-(CR^*R^*)_{r+s}-$, $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

(iv) R^3 and R^{4*} together designate a biradical selected from $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

(v) R^3 and R^5 together designate a biradical selected from $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$; or

(vi) R^{1*} and R^{4*} together designate a biradical selected from $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

(vii) R^{1*} and R^{2*} together designate a biradical selected from $-(CR^*R^*)_r-O-(CR^*R^*)_s-$, $-(CR^*R^*)_r-S-(CR^*R^*)_s-$, and $-(CR^*R^*)_r-N(R^*)-(CR^*R^*)_s-$;

wherein each R^* is independently selected from hydrogen, halogen, azido, cyano, nitro, hydroxy, mercapto, amino, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and/or two adjacent (non-geminal) R^* may together designate a double bond, and each of r and s is 0-3 with the proviso that the sum r+s is 1-4;

each of the substituents R^{1*}, R^2, R^{2*}, R^3, R^{4*}, R^5, and R^{5*}, which are not involved in Q, Q* or the biradical, is independently selected from hydrogen, optionally substituted C_{1-12}-alkyl, optionally substituted C_{2-12}-alkenyl, optionally substituted C_{2-12}-alkynyl, hydroxy, C_{1-12}-alkoxy, C_{2-12}-alkenyloxy, carboxy, C_{1-12}-alkoxycarbonyl, C_{1-12}-alkylcarbonyl, formyl, aryl, aryloxy-carbonyl, aryloxy, arylcarbonyl, heteroaryl, heteroaryloxy-carbonyl, heteroaryloxy, heteroarylcarbonyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, amino-C_{1-6}-alkyl-aminocarbonyl, mono- and di(C_{1-6}-alkyl)amino-C_{1-6}-alkyl-aminocarbonyl, C_{1-6}-alkylcarbonylamino, carbamido, C_{1-6}-alkanoyloxy, sulphono, C_{1-6}-alkylsulphonyloxy, nitro, azido, sulphanyl, C_{1-6}-alkylthio, halogen, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, where aryl and heteroaryl may be optionally substituted, and where two geminal substituents together may designate oxo, thioxo, imino, or optionally substituted methylene, or together may form a spiro biradical consisting of a 1-5 carbon atom(s) alkylene chain which is optionally interrupted and/or terminated by one

or more heteroatoms/groups selected from -O-, -S-, and -(NR^N)- where R^N is selected from hydrogen and C_{1-4}-alkyl, and where two adjacent (non-geminal) substituents may designate an additional bond resulting in a double bond; and R^{N*}, when present and not involved in a biradical, is selected from hydrogen and C_{1-4}-alkyl;

and basic salts and acid addition salts thereof;

with the first proviso that,

(i) R^3 and R^5 do not together designate a biradical selected from -CH_2-CH_2-, -O-CH_2-, and -O-Si(^{i}Pr)$_2$-O-Si(^{i}Pr)$_2$-O-;

and with the second proviso that any chemical group (including any nucleobase), which is reactive under the conditions prevailing in oligonucleotide synthesis, is optionally functional group protected.

61. A nucleoside analogue according to claim 60, wherein the group B is selected from nucleobases and functional group protected nucleobases.

62. A nucleoside analogue according to claim 60, wherein X is selected from -O-, -S-, and -$N(R^{N*})$-.

63. A nucleoside analogue according to claim 60, wherein each of the substituents R^{1*}, R^2, R^{2*}, R^3, R^{3*}, R^{4*}, R^5, and R^{5*}, which are present and not involved in Q, Q^* or the biradical, is independently selected from hydrogen, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, hydroxy, C_{1-6}-alkoxy, C_{2-6}-alkenyloxy, carboxy, C_{1-6}-alkoxycarbonyl, C_{1-6}-alkylcarbonyl, formyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, azido, C_{1-6}-alkanoyloxy, sulphono, sulphanyl, C_{1-6}-alkylthio, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, and halogen, where two geminal substituents together may designate oxo, and where R^{N*}, when present and not involved in a biradical, is selected from hydrogen and C_{1-4}-alkyl, with the proviso that

any hydroxy, amino, mono(C_{1-6}-alkyl)amino, sulfanyl, and carboxy is optionally protected.

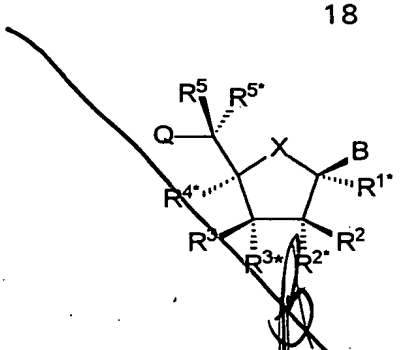
64. A nucleotide analogue according to claim 60, each of the substituents R^{1*}, R^2, R^{2*}, R^3, R^{3*}, R^{4*}, and R^5, R^{5*}, R^6, R^{6*}, which are present and not involved in Q^* or the biradical, designate hydrogen.

65. A nucleoside analogue according to claim 60, wherein R^{3*} designates P^*.

66. A nucleoside analogue according to claims 60, wherein Q is independently selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Prot-O-, mercapto, Prot-S-, C_{1-6}-alkylthio, amino, Prot-N(R^H)-, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyl, optionally substituted C_{2-6}-alkynyloxy, monophosphate, diphosphate, triphosphate, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, carboxy, sulphono, hydroxymethyl, Prot-O-CH_2-, aminomethyl, Prot-N(R^H)-CH_2-, carboxymethyl, sulphonomethyl, where Prot is a protection group for -OH, -SH, and -NH(R^H), respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl; and

Q^* is selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Act-O-, mercapto, Act-S-, C_{1-6}-alkylthio, amino, Act-N(R^H)-, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyl, optionally substituted C_{2-6}-alkynyloxy, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, carboxy, sulphono, where Act is an activation group for -OH, -SH, and -NH(R^H), respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl.

67. A nucleotide analogue according to claim 60, having the general formula IIa



IIa

wherein the substituents Q, B, R^{1*}, R^2, R^{2*}, R^3, R^{3*}, R^{4*}, R^5, and R^{5*} are as defined in claims 60.

68. A nucleoside analogue according to claim 67, wherein R^{3*} designates P^*.

69. A nucleoside analogue according to claim 68, wherein R^{2*} and R^{4*} together designate a biradical.

70. A nucleoside analogue according to claim 69, wherein X is O, R^2 selected from hydrogen, hydroxy, and optionally substituted C_{1-6}-alkoxy, and R^{1*}, R^3, R^5, and R^{5*} designate hydrogen.

71. A nucleoside analogue according to claim 70, wherein the biradical is selected from -O-, $-(CH_2)_{0-1}-O-(CH_2)_{1-3}-$, $-(CH_2)_{0-1}-S-(CH_2)_{1-3}-$, and $-(CH_2)_{0-1}-N(R^N)-(CH_2)_{1-3}-$.

72. A nucleoside analogue according to claim 71, wherein the biradical is selected from $-O-CH_2-$, $-S-CH_2-$ and $-N(R^N)-CH_2-$.

73. A nucleoside analogue according to claim 69, wherein B is selected from nucleobases.

74. A nucleoside analogue according to claim 73, wherein the oligomer comprises at least one LNA wherein B is selected from adenine and guanine and at least one LNA wherein B is selected from thymine, cytosine and urasil.

75. A nucleoside analogue according to claim 70, wherein the biradical is $-(CH_2)_{2-4}-$.

76. A nucleoside analogue according to claim 68, wherein R^2 and R^3 together designate a biradical.

77. A nucleoside analogue according to claim 76, wherein X is O, R^{2*} is selected from hydrogen, hydroxy, and optionally substituted C_{1-6}-alkoxy, and R^{1*}, R^{4*}, R^5, and R^{5*} designate hydrogen.

78. A nucleoside analogue according to claim 77, wherein the biradical is $-(CH_2)_{0-1}-O-(CH_2)_{1-3}-$.

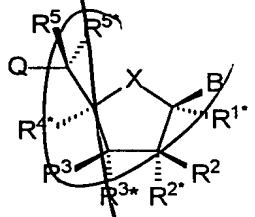
79. A nucleoside analogue according to claim 77, wherein the biradical is $-(CH_2)_{1-4}-$.

80. A nucleoside analogue according to claim 68, wherein one R^* is selected from hydrogen, hydroxy, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and any remaining substituents R^* are hydrogen.

81. A nucleoside analogue according to claim 68, wherein a group R^* in the biradical of at least one LNA is selected from DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands.

82. A nucleoside analogue according to claim 68, wherein the LNA(s) has/have the general formula Ia.

83. A nucleoside analogue according to claim 60 of the general formula IIa



IIa

wherein X is -O-;

B is selected from nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

R^{3*} is a group Q*;

each of Q and Q* is independently selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Prot-O-, Act-O-, mercapto, Prot-S-, Act-S-, C_{1-6}-alkylthio, amino, Prot-$N(R^H)$-, Act-$N(R^H)$-, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyl, optionally substituted C_{2-6}-alkynyloxy, monophosphate, diphosphate, triphosphate, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, carboxy, sulphono, hydroxymethyl, Prot-O-CH_2-, Act-O-CH_2-, aminomethyl, Prot-$N(R^H)$-CH_2-, Act-$N(R^H)$-CH_2-, carboxymethyl, sulphonomethyl, where Prot is a protection group for -OH, -SH, and -$NH(R^H)$, respectively, Act is an activation group for -OH, -SH, and -$NH(R^H)$, respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl;

R^{2*} and R^{4*} together designate a biradical selected from -O-, -S, -$N(R^*)$-, -$(CR^*R^*)_{r+s+1}$-, -$(CR^*R^*)_r$-O-$(CR^*R^*)_s$-, -$(CR^*R^*)_r$-S-$(CR^*R^*)_s$-, -$(CR^*R^*)_r$-$N(R^*)$-$(CR^*R^*)_s$-, -O-$(CR^*R^*)_{r+s}$-O-, -S-$(CR^*R^*)_{r+s}$-O-, -O-$(CR^*R^*)_{r+s}$-S-, -$N(R^*)$-$(CR^*R^*)_{r+s}$-O-, -O-$(CR^*R^*)_{r+s}$-$N(R^*)$-, -S-$(CR^*R^*)_{r+s}$-S-, -$N(R^*)$-$(CR^*R^*)_{r+s}$-$N(R^*)$-, -$N(R^*)$-$(CR^*R^*)_{r+s}$-S-, and -S-$(CR^*R^*)_{r+s}$-$N(R^*)$-; wherein each R^* is independently selected from hydrogen, halogen, azido, cyano, nitro, hydroxy, mercapto, amino, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and/or two adjacent (non-geminal) R^* may together designate a double bond, and each of r and s is 0-3 with the proviso that the sum r+s is 1-4;

each of the substituents R^{1*}, R^2, R^3, R^5, and R^{5*} is independently selected from hydrogen, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, hydroxy, C_{1-6}-alkoxy, C_{2-6}-alkenyloxy, carboxy, C_{1-6}-alkoxycarbonyl, C_{1-6}-alkylcarbonyl, formyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, azido, C_{1-6}-alkanoyloxy, sulphono,

sulphanyl, C_{1-6}-alkylthio, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and halogen, where two geminal substituents together may designate oxo;

and basic salts and acid addition salts thereof;

and with the proviso that any chemical group (including any nucleobase), which is reactive under the conditions prevailing in oligonucleotide synthesis, is optionally functional group protected.

84. A nucleotide analogue according to claim 83, wherein one R^* is selected from hydrogen, hydroxy, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and any remaining substituents R^* are hydrogen.

85. A nucleotide analogue according to claim 83, wherein the biradical is selected from -O-, $-(CH_2)_{0-1}-O-(CH_2)_{1-3}-$, $-(CH_2)_{0-1}-S-(CH_2)_{1-3}-$, $-(CH_2)_{0-1}-N(R^N)-(CH_2)_{1-3}-$, and $-(CH_2)_{2-4}-$.

86. A nucleoside analogue according to claim 85, wherein the biradical is selected from $-O-CH_2-$, $-S-CH_2-$ and $-N(R^N)-CH_2-$.

87. A nucleoside analogue according to claim 83, wherein B is selected from nucleobases.

88. A nucleoside analogue according to claim 87, wherein the oligomer comprises at least one LNA wherein B is selected from adenine and guanine and at least one LNA wherein B is selected from thymine, cytosine and urasil.

89. A nucleoside analogue according to claim 83, wherein B designates a nucleobase, X is -O-, R^{2*} and R^{4*} together designate a biradical selected from $-(CH_2)_{0-1}-O-(CH_2)_{1-3}-$, $-(CH_2)_{0-1}-S-(CH_2)_{1-3}-$, and $-(CH_2)_{0-1}-N(R^N)-(CH_2)_{1-3}-$ where R^N is selected from hydrogen and C_{1-4}-alkyl, Q designates Prot-O-, R^{3*} is Q^* which designates Act-OH, and R^{1*}, R^2,

R^3, R^5, and R^{5*} each designate hydrogen, wherein Act and Prot are as defined in claim 58.

90. A nucleoside analogue according to claim 83, wherein B designates a nucleobase, X is -O-, R^{2*} and R^{4*} together designate a biradical selected from $-(CH_2)_{0-1}-O-(CH_2)_{1-3}-$, $-(CH_2)_{0-1}-S-(CH_2)_{1-3}-$, and $-(CH_2)_{0-1}-N(R^N)-(CH_2)_{1-3}-$ where R^N is selected from hydrogen and C_{1-4}-alkyl, Q is selected from hydroxy, mercapto, C_{1-6}-alkylthio, amino, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyloxy, monophosphate, diphosphate, and triphosphate, R^{3*} is Q^* which is selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, mercapto, C_{1-6}-alkylthio, amino, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyl, and optionally substituted C_{2-6}-alkynyloxy, R^3 is selected from hydrogen, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, and optionally substituted C_{2-6}-alkynyl, and R^{1*}, R^2, R^5, and R^{5*} each designate hydrogen.

91. A nucleoside analogue according to claim 83, wherein B designates a nucleobase, X is -O-, R^2 and R^3 together designate a biradical selected from $-(CH_2)_{0-1}-O-CH=CH-$, $-(CH_2)_{0-1}-S-CH=CH-$, and $-(CH_2)_{0-1}-N(R^N)-CH=CH-$ where R^N is selected from hydrogen and C_{1-4}-alkyl, Q is selected from hydroxy, mercapto, C_{1-6}-alkylthio, amino, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyloxy, monophosphate, diphosphate, and triphosphate, R^{3*} is Q^* which is selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, mercapto, C_{1-6}-alkylthio, amino, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyl, and optionally substituted C_{2-6}-alkynyloxy, and R^{1*}, R^{2*}, R^{4*}, R^5, and R^{5*} each designate hydrogen.

92. A nucleoside analogue according to claim 60, which is selected from *(1R,3R,4R,7S)*-7-(2-cyanoethoxy(diisopropylamino)phosphinoxy)-1-(4,4'-dimethoxytrityloxymethyl)-3-(thymin-1-yl)-2,5-dioxabicyclo[2.2.1]heptane, *(1R,3R,4R,7S)*-7-hydroxy-1-(4,4'-dimethoxytrityloxymethyl)-3-(thymin-1-yl)-2,5-

dioxabicyclo[2.2.1]heptane-7-*O*-(2-chlorophenylphosphate), and (*1R,3R,4R,7S*)-7-hydroxy-1-(4,4'-dimethoxytrityloxymethyl)-3-(thymin-1-yl)-2,5-dioxabicyclo[2.2.1]heptane-7-*O*-(*H*-phosphonate) and the 3-(cytosin-1-yl), 3-(urasil-1-yl), 3-(adenin-1-yl) and 3-(guanin-1-yl) analogues thereof

93. A method of using an LNA as defined in claim 60 for the preparation of an LNA modified oligonucleotide (an oligomer) as defined in claim 1.

94. A method according to claim 93, wherein the LNA modified oligonucleotide comprises normal nucleosides as well as modified nucleosides different from those defined in claim 60.

95. A method according to claim 93, wherein the incorporation of LNA modulates the ability of the oligonucleotide to act as a substrate for nucleic acid active enzymes.

96. A method of using of an LNA as defined in claim 60 for the preparation of a conjugate of an LNA modified oligonucleotide and a compound selected from proteins, amplicons, enzymes, polysaccharides, antibodies, haptens, peptides, and PNA.

97. A conjugate of an LNA modified oligonucleotide (an oligomer) as defined in claim 1 and a compound selected from proteins, amplicons, enzymes, polysaccharides, antibodies, haptens, peptides, and PNA.

98. A method of using an LNA as defined in claim 60 as a substrate for enzymes active on nucleic acids.

99. A method according to claim 98, wherein the substituent Q in the formula I in claim 60 designates a triphosphate.

100. A method according to claim 98, wherein the LNA is used as a substrate for DNA and RNA polymerases.

101. A method of using an LNA as defined in claim 60 as a therapeutic agent.

102. A method of using an LNA as defined in claim 60 for diagnostic purposes.

103. A solid support material having immobilised thereto an optionally nucleobase protected and optionally 5'-OH protected LNA.

104. A method of using one or more LNA as defined in claim 60 in the construction of solid surface onto which LNA modified oligonucleotides of different sequences are attached .

105. A method according to claim 113, wherein the LNA modified oligonucleotides are attached in a predetermined pattern.

106. A method according to claim 113, wherein the LNAs are used to equalise the T_m of the corresponding unmodified reference oligonucleotides.

107. A method according to claim 113, wherein the LNA modified oligonucleotides have an increased affinity toward complementary ssDNA or ssRNA compared to native oligonucleotide.

108. A method according to claim 113, wherein the LNA modified oligonucleotides have an increased specificity toward complementary ssDNA or ssRNA compared to native oligonucleotide.

109. A method of using LNA modified oligomers (ribozymes) as defined in claim 1 in the sequence specific cleavage of target nucleic acids.

110. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 in therapy.

111. A method according to claim 110, wherein the LNA modified oligonucleotide recruits RNAseH.

112. A method of using complexes of more than one LNA modified oligonucleotide (an oligomer) as defined in claim 1 in therapy.

113. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 as an aptamer in therapeutic applications.

114. A method according to claim 119 , wherein the LNA modified oligonucleotide comprises at least one internucleoside linkage not being a phosphate diester linkage.

115. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 in diagnostics.

116. A method according to claim 115, wherein the oligonucleotide comprises a photochemically active group, a thermochemically active group, a chelating group, a reporter group, or a ligand that facilitates the direct of indirect detection of the oligonucleotide or the immobilisation of the oligonucleotide onto a solid support.

117. A method according to claim 116, wherein the photochemically active group, the thermochemically active group, the chelating group, the reporter group, or the ligand includes a spacer (K), said spacer comprising a chemically cleavable group.

118. A method according to claim 116, wherein the photochemically active group, the thermochemically active group, the chelating group, the reporter group, or the ligand is attached via the biradical (i.e. as R) of at least one of the LNA(s) of the oligonucleotide.

119. A method according to claim 115 for capture and detection of naturally occurring or synthetic double stranded or single stranded nucleic acids.

120. A method according to claim 115 for purification of naturally occurring double stranded or single stranded nucleic acids.

121. A method according to claim 115 as a probe in in-situ hybridisation, in Southern hydridisation, Dot blot hybridisation, reverse Dot blot hybridisation, or in Northern hybridisation.

122. A method according to claim 115 in the construction of an affinity pair.

123. A method according to claim 115 as a primer in a nucleic acid sequencing reaction or primer extension reactions.

124. A method according to claim 115 as a primer in a nucleic acid amplification reaction.

125. A method according to claim 124, wherein the primer is so adapted that the amplification reaction is an essentially linear reaction.

126. A method according to claim 124, wherein the primer is so adapted that the amplification reaction is an essentially exponential reaction.

127. A method according to claim 124, wherein the nucleic acid amplification reaction results in a double stranded DNA product comprising at least one single stranded end.

128. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 as an aptamer in molecular diagnostics.

129. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 as an aptamer in RNA mediated catalytic processes.

130. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 as an aptamer in specific binding of antibiotics, drugs, amino acids, peptides, structural proteins, protein receptors, protein enzymes, saccharides, polysaccharides, biological cofactors, nucleic acids, or triphosphates.

131. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 as an aptamer in the separation of enantiomers from racemic mixtures by stereospecific binding.

132. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 for the labelling of cells.

133. A method according to claim 132, wherein the label allows the cells to be separated from unlabelled cells.

134. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 to hybridise to non-protein coding cellular RNAs *in vivo* or *in-vitro*.

135. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 in the construction of an oligonucleotide containing a fluorophor and a quencher, positioned in such a way that the hybridised state of the oligonucleotide can be distinguished from the unbound state of the oligonucleotide by an increase in the fluorescent signal from the probe.

136. A method of using an LNA modified oligonucleotide (an oligomer) as defined in claim 1 in the construction of Taqman probes or Molecular Beacons.

137. A kit for the isolation, purification, amplification, detection, identification, quantification, or capture of natural or synthetic nucleic acids, the kit comprising a reaction body and one or more LNA modified oligonucleotides (oligomer) as defined in claim 1.

138. A kit according to claim 137, wherein the LNA modified oligonucleotides are immobilised onto said reactions body.

139. A kit for the isolation, purification, amplification, detection, identification, quantification, or capture of natural or synthetic nucleic acids, the kit comprising a reaction body and one or more LNAs as defined in claim 60.

140. A kit according to claim 139, wherein the LNAs are immobilised onto said reactions body.

add C'